

# Analysis Challenges 'Placebo Effect'

Danish Study May Affect Research and Treatment Decisions

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Surprising new evidence has called into question the existence of the "placebo effect," the widely accepted principle that people with various illnesses will often improve if given a dummy pill or a sham treatment.

For a half-century, doctors have been taught that this phenomenon is partly responsible for drugs' effectiveness. Researchers have taken it into account when testing new medicines. Biologists and psychologists have searched for its cause. Ethicists have even debated whether doctors could justifiably deceive patients to take advantage of it.

But in the most comprehensive effort yet to evaluate whether placebos work, Danish researchers conclude that they have little effect after all and should not be used outside research settings. Their analysis examined 114 studies of various symptoms or disorders and found that the placebos were no better than no treatment for most of the problems studied. Placebos did appear to produce modest benefit in studies of pain and in some other studies where the outcome being measured was similarly subjective.

The ethics of placebo use -- both in medical practice and in research -- have been hotly debated in recent years. In addition, proponents of alternative therapies often point to patients' response to placebos as evidence of the mind's power to heal, and much research has focused on understanding and possibly harnessing that response.

"I'm surprised by this," said David Spiegel, a professor of psychiatry at Stanford University School of Medicine. "What this shows is not that [the placebo effect] doesn't exist, but that it doesn't answer all problems. We need to look more carefully at effective and ineffective components" of the response to placebos.

The report should change the way doctors make decisions about treatment, said John C. Bailar III, a professor emeritus of health studies at the University of Chicago who wrote an editorial accompanying the study in today's issue of *The New England Journal of Medicine*.

"Now. . . anybody who says there is a placebo effect has the burden of proof," Bailar said. "I think it's going to have quite a substantial effect on how medicine is practiced, particularly non-research medicine."

Doctors give a placebo whenever they prescribe a drug merely to placate a patient, without any evidence that it is necessary or effective, Bailar noted. "I think placebos are used all over the place," he said. "An outstanding example is the prescription of antibiotics for the common cold, which is a viral disease" and therefore unaffected by antibiotics.

The idea that placebos have a powerful, scientifically measurable effect dates from a 1955 medical article by Henry Beecher. Beecher claimed that in 15 clinical trials, roughly one-third of patients responded to a dummy treatment. To take this phenomenon into account, he argued, researchers should evaluate new drugs by testing them against a placebo in clinical trials.

In the decades since, people have come to equate the "placebo effect" with the positive change often observed in patients given a placebo in such studies. But such patients may improve for many other reasons, such as the tendency of most illnesses to resolution on their own or the wish to please the doctor by reporting benefits from treatment.

"It doesn't make any sense to call it a 'placebo effect' as if you imply some kind of causal relation," said Asbjørn Hróbjartsson of the University of Copenhagen and the Nordic Cochrane Centre, the new study's principal author.

To investigate whether dummy treatments could be beneficial, Hróbjartsson and colleague Peter C. Goetzsche undertook an international computer search for studies done since the 1940s in which some participants were randomly assigned to receive a placebo and others were assigned to get no treatment. They analyzed outcomes of 114 randomized trials involving 8,525 participants with diverse medical problems. The placebo could be a dummy drug, a physical manipulation or a psychological intervention such as a conversation. Outcomes could be either binary (for instance, presence or absence of infection) or continuous (such as partial improvement in a symptom).

The study was done as part of the Cochrane Collaboration, a loose-knit international association of researchers and statisticians whose goal is to extract "bottom-line" information from the often contradictory results of published medical studies.

Compared with no treatment, placebos had no significant effect either on binary outcomes or on continuous outcomes where the result was measurable (such as weight loss). Placebos appeared to produce some benefit only in studies with continuous outcomes that were subjective -- that is, reported by the patient. Among individual conditions, only pain showed evidence of a modest but significant placebo response.

Even for pain, "I'm very much in doubt" whether the effect is real, Hróbjartsson said. "The difference between placebo and no treatment could also reflect reporting bias" on the part of study participants.

There is fairly good evidence from other research that placebos can relieve pain, but little proof that they work for other conditions, said Robert J. Temple, director of medical policy at the Food and Drug Administration's Center for Drug Evaluation and Research.

"I think it's a terrific thing to have done," he said of the Danish study, "but I have to tell you I'm not the least bit surprised" by the conclusions.

Temple noted that the report does not address placebos' role in studies to test new treatments. Typically, one group of participants receives an experimental drug and another group receives a dummy pill that looks identical. This strategy prevents participants and researchers from knowing who is getting the drug, thus avoiding bias that might influence the results.

Most experts consider such studies ethical provided that participants understand that they may receive a placebo and that participants are not harmed by being denied an effective treatment for a serious disease.

Ted J. Kaptchuk, an assistant professor of medicine at Harvard Medical School who has done extensive research on placebos, said some other evidence contradicts the Danish study's conclusion that placebos are ineffective.

"There have been several studies that compare two different kinds of placebo, like a needle versus a pill," Kaptchuk said. "They consistently show that a device has a bigger effect than a pill. If a placebo has no effect, [changing the kind of placebo used] should have no effect."

*Staff writer David Brown contributed to this report.*

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